Abstracts

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Family Members of Patients with Abdominal Aortic Aneurysms Are at Increased Risk for Aneurysms: Analysis of 618 Probands and Their Families from the Liège AAA Family Study

Sakalihasan N, Defraigne JO, Kerstenne MA, et al. Ann Vasc Surg 2014;28:787-97.

Conclusion: Aggregation of AAA in families, particularly among brothers, provides rational for targeted screening studies in relatives of patients with AAA.

Summary: Aggregation of AAA in families has been reported since the 1970's, with the largest collection of 233 AAA families published in 2003 (Kuivaniemi H et al, J Vasc Surg 2003;37:340-5). Familial clustering of AAA has also been documented in twin studies (Wahlgren CM et al, J Vasc Surg 2010;51:3-7). In this study the authors sought to analyze the results of the Liège AAA Family Study that consists of 618 patients with unrelated AAA, diagnosed at the University Hospital of Liège. They sought to answer the following questions: (1) What percentage of patients with AAA (referred as "AAA probands") had a positive family history for AAA? (2) What is the prevalence of AAA among the relatives of AAA probands? (3) Do familial AAA (FAAA) cases differ from nonfamilial (sporadic) AAA cases in clinical characteristics? The study consisted of patients with unrelated AAA from the period of 1999 and 2012, diagnosed at University Hospital of Liège Belgium. A detailed family history was obtained from interviews and recorded using Progeny software. The 618 identified patients were divided into 2 study groups; Group I: 296 patients with AAA (268; 91% men) were followed with computerized tomography combined with positron emission tomography; and Group II: 322 patients with AAA probands (295; 92% men) whose families were invited to ultrasonographic screening. In the initial interviews 62 (10%) of the 618 patients with AAA reported a positive family history for AAA. Ultrasound screening identified 24 new AAA's among 186 relatives (≥50 years) of 144 families yielding an AAA prevalence of 13%. The highest prevalence (25%) was found among brothers. By combining the number of AAA's found by ultrasound screening with those diagnosed previously, the observed lifetime prevalence of AAA was estimated to be 32% in brothers. The familial AAA cases were more likely to have a ruptured AAA than the sporadic cases (8% vs 2.4%; $P < .0001$).

Comment: While we already know there is a genetic component to AAA etiology, the current data highlights the fact that brothers of AAA patients are those at highest risk. In fact because of the limitations of interviews, the prevalence of AAA among family members and brothers of patients with AAA may actually be underestimated by this and previous studies of the genetic component of AAA etiology. Given what appears to be higher propensity for rupture of familial AAA cases, and the high risk among brothers, it does seem that the author's conclusion that targeted screening of the brothers of patients with AAA is reasonable. In addition, given the high prevalence among brothers, it seems that the screening for AAAs in brothers of patients with AAA should not have to wait until the brother reaches 65 years of age.

Thrombolysis for Pulmonary Embolism and Risk of All-Cause Mortality, Major Bleeding, and Intracranial Hemorrhage: A Meta-Analysis

Chatterjee S, Chakraborty A, Weinberg I, et al. JAMA 2014;311:2414-21.

Conclusions: Among patients with pulmonary embolism (PE), including those who were hemodynamically stable with right ventricular dysfunction, thrombolytic therapy was associated with lower rates of all-cause mortality and increased risks of major bleeding and intracranial hemorrhage.

Summary: It seems logical that thrombolytic therapy may be beneficial in the treatment of some patients with PE. However, to date there has been no individual study with adequate statistical power to determine whether thrombolytic therapy is associated with improved survival in comparison to conventional anticoagulation. The purpose of the author's paper was to perform a meta-analysis to determine the mortality benefits and bleeding risks associated with thrombolytic therapy compared with anticoagulation in acute PE, including the subset of patients hemodynamically stable but with right ventricular dysfunction, so called intermediate-risk PE. The authors searched PubMed, the Cochrane Library, EMBASE, EBSCO, Web of Science, and CINAHL databases from their inception through April 10, 2014. Patients were eligible for inclusion in this meta-analysis if they were in randomized trials comparing thrombolytic therapy to standard anticoagulant therapy in PE patients. There were sixteen trials encompassing 2115 individuals identified. Eight trials comprising 1775 patients specified inclusion of patients with intermediate-risk PE. The data was independently extracted by two reviewers and included number of patients, patient characteristics, duration of follow-up and outcomes. Primary outcomes were all-cause mortality and major bleeding. Secondary outcomes were risk of recurrent embolism and intracranial hemorrhage (ICH). Peto odds ratio (OR) estimates and associated 95% CIs were calculated using a fixed-effects model. Use of thrombolytics was associated with lower all-cause mortality (OR, 0.53; 95% CI, 0.32-0.88; 2.17% [23/1061] vs 3.89% [41/1054] with anticoagulants. The number needed to treat [NNT] = 59) and greater risks of major bleeding (OR, 2.73; 95% CI, 1.91-3.91; 9.24% [98/1061] vs 3.42% [36/1054]; number needed to harm [NNH] = 18) and ICH (OR, 4.63; 95% CI, 1.78-12.04; 1.46% [15/1024] vs 0.19% [2/1019]; NNH = 78). Major bleeding was not significantly increased in patients 65 years and younger (OR, 1.25; 95% CI, 0.50-3.14). Thrombolysis was associated with a lower risk of recurrent PE (OR, 0.40; 95% CI, 0.22-0.74; 1.17% [12/1024] vs 3.04% [31/1019]; NNT = 54). In intermediate-risk PE trials, thrombolysis was associated with lower mortality (OR, 0.48; 95% CI, 0.25-0.92) but more major bleeding events (OR, 3.19; 95% CI, 2.07-4.92).

Comment: The authors indicate that to the author's knowledge, this is the first analysis of thrombolysis for treatment of PE that has sufficient statistical power to detect associations with meaningful mortality reduction, including hemodynamically stable patients with right ventricular dysfunction. However, if so, then improvement in mortality must be tempered by what appears to be significantly increased risk of major bleeding and intracranial hemorrhage with use of thrombolytic therapy for PE, particularly in patients older than 65 years of age.

Vena Cava Filters in Unstable Elderly Patients With Acute Pulmonary Embolism

Stein PD, Matta F. Am J Med 2014;127:222-5.

Conclusions: Vena cava filers are associated with a reduced in-hospital, all-cause case fatality rate in unstable adults with pulmonary embolism (PE), irrespective of age.

Summary: Data from the Nationwide Inpatient Sample suggest inferior vena cava filters can be associated with a reduced in-hospital all-cause fatality rate in unstable patients with acute PE (Stein PD et al, Am J Med 2012;125:478-84). The purpose of this paper was to additionally investigate whether vena cava filters are associated with a reduced case fatality rate in adults of all ages with unstable PE, particularly the elderly.

The authors again utilized the Nationwide Inpatient Sample for their data. They identified patients with PE who were unstable (in shock or ventilator dependent) from 1999 to 2008 from the Nationwide Inpatient Sample. There were 21,095 unstable patients with PE who received thrombolytic therapy. In these patients in-hospital all-cause fatality rate was lower in every age group who received a vena cava filter in addition to thrombolytic therapy ($P = .0012$ to $< .0001$). Patients aged >81 years showed the greatest absolute reduction of case fatality rate with filters (19%). Among 50,210 unstable patients who did not receive thrombolytic therapy, case fatality rate also was lower in every age group who received a vena cava filter (all $P < .0001$). Patients aged ≥81 years with vena cava filters showed the greatest absolute risk reduction of case fatality rate (27.7%).

Comment: Vena cava filters remain technology in search of proven benefit. While administrative databases such as the Nationwide Inpatient Sample are clearly not perfect, they may provide more useful data then that from individual case series. This data at least provides some justifications for use of vena cava filters in unstable patients with PE requiring